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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,836	03/30/2006	Angelo Guglielmotti	281760US0PCT	6824

22850 7590 03/24/2008
OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C.
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EXAMINER

RAMACHANDRAN, UMAMAHESWARI

ART UNIT	PAPER NUMBER
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1617

NOTIFICATION DATE	DELIVERY MODE
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03/24/2008

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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<p align="center">Advisory Action Before the Filing of an Appeal Brief</p>	Application No. 10/560,836	Applicant(s) GUGLIELMOTTI ET AL.	
	Examiner UMAMAHESWARI RAMACHANDRAN	Art Unit 1617	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 21 February 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
 b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
 (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
 (b) ☐ They raise the issue of new matter (see NOTE below);
 (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
 5. ☐ Applicant's reply has overcome the following rejection(s): _____.
 6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
 7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
 The status of the claim(s) is (or will be) as follows:
 Claim(s) allowed: _____.
 Claim(s) objected to: _____.
 Claim(s) rejected: 6-24.
 Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
 9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
 10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
 12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____.
 13. ☐ Other: _____.

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1617

Note: The amendment will be entered but the claims are not allowable for the following reasons.

Claim 6 has been amended and claim 24 has been added new by the amendment dated 2/12/008. Applicants' arguments regarding the rejections have been fully considered and found not to be persuasive.

The rejection of claims 6 and 13 under U.S.C 112(1) will be withdrawn due to the amendment of claim 6.

The new claim 24 will be rejected under U.S.C 112(1) written description for the same reasons as given in the final rejection for claims 6 and 13 (9/12/2007). The specification clearly teaches that R is cyclohexyl prepared according to examples 23 of EPA-630376. According to example 23 of the document EPA-630376, the reference teaches the addition of an alkyl bromide to E21 compound. The alkyl bromide can be cyclohexyl or cyclohexylmethyl bromide. Also, claim set 1 (claim 5) and claim set 2 (claim 5) clearly indicates that R is a cyclohexyl group. It is clearly implied from the specification that compound of formula I with R being cyclohexyl prepared according to the method in example 23. Hence it is a new matter and does not have support in the specification.

Claim 13 will be rejected under U.S.C 112(2) for not having an antecedent basis.

Claims 6-12, 14-17 will be rejected under U.S.C. 103 as being unpatentable over Gaster et al. in view of Burstein et al. and Kayser et al. (British J of Pharmacology, 2002, 137, 1287-1297) and further in view of Journ et al.

Gaster teach the compounds of the instant invention as serotonin receptor antagonists (5-HT₄) and further teach their use in migraine. Burstein et al. teach most migraine patients exhibit cutaneous allodynia during a fully developed migraine attack. Kayser teach that hyperalgesia and allodynia of the face and the scalp often accompany migraine headache (p 1288, lines 26-20) and further teach that antimigraine 5-HT_{1B/1D} serotonin receptor agonist exerted anti-allodynic effects in the rat model of trigeminal neuropathic pain (p 1295, conclusion). Jorum teach that allodynia and hyperalgesia as clinical findings of neuropathic pain. Hence it would have been obvious to one of ordinary skill in the art at the time of the invention to administer compounds of the instant invention in the treatment of neuropathic pain in a disorder such as migraine because of the teachings of Gaster, Burstein and Kayser. Gaster teaches that the compounds are useful in the treatment of migraine, Burstein et al. teach most migraine patients exhibit cutaneous allodynia during a fully developed migraine attack and Kayser clearly teaches that hyperalgesia and allodynia (clinical findings of neuropathic pain) of the face and the scalp often accompany migraine headache. One having ordinary skill in the art would have been motivated to use the compounds in the treatment of neuropathic pain in expectation of success because migraine is often accompanied by hyperalgesia and allodynia as taught by the prior art and the compounds of the instant invention has been shown to be useful in the treatment of migraine.

The remaining claims 18-23 will be rejected based on the above rejection and with the previously applied references that was applied to reject these claims. Please refer to the final office action for the rejection of claims 18-23.